DETAILED ACTION

Examiner acknowledges Applicants' reply, filed July 14, 2008. Claim 65 is cancelled and claim 67 is amended.

Claims 22-27, 29-57, 59, 62-64, 66 and 67 are pending in this application. Claims 22-26 and 30-57 are direct to non-elected inventions and apparently were withdrawn from consideration pursuant to 37 CFR 1.142(b) in the Office Action dated July 13, 2005.

Claims 27, 29, 59, 62-64, 66 and 67 are under examination.

This application was filed on April 16, 2002, pursuant to 35 U.S.C. § 371, thereby obtaining priority to international application number PCT/JP00/03413, filed May 26, 2000.

Specification

The amendments to the Specification filed July 14, 2008, are objected to under 35 U.S.C. 132(a) for introducing new matter into the disclosure. Specifically:

In the amendment to the paragraph beginning at page 3, line 11:

1. addition of new object "sera samples";
2. deletion of object "blood samples";
3. deletion of object "plurality of installations" (emphasis mine).

In the amendment to the paragraph beginning at page 4, line 2:

1. deletion of step of "obtaining";

2. addition of object “prepared” reconstructed lipoprotein;
3. deletion of steps of freeze-drying and stabilizing “in the presence of a stabilizer”.

In the amendment to the paragraph beginning at page 5, line 4:

1. deletion of step of incorporating “into [object]”;
2. addition of step of oxidizing phospholipid “into lipoproteins of blood plasma”.

In the amendment to the paragraph beginning at page 5, line 28:

1. deletion of step of “oxidizing” lipoproteins;
2. deletion of step of oxidizing “lipoproteins as egg yolk, milk, whole blood[...]”;
3. deletion of step of “acetylating” lipoproteins;
4. deletion of step of “reacting” lipoproteins.

Applicants are required to cancel new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27, 29, 59, 62-64, 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimura *et al*. (PTO 07-6676, English translation of JP 09-2881064) in view of Proksch & Bonderman (US 4,216,117).

Kimura *et al*. describe a method for producing a denatured lipoprotein standard (see Title, "lipoprotein oxide and standard substance").

Kimura *et al*. do not teach the claimed steps of: freezing, melting, mixing and freeze-drying.

However, Proksch & Bonderman describe:

1. freezing a first solution containing lipoproteins (see *e.g.*, col. 3, line 59, "serum which is frozen[...]"; see *also*, col. 6, lines 35-36, "serum which has been frozen[...]") (paraphrasing mine);

2. melting the frozen solution (see *e.g.*, col. 3, line 59, "serum which is[…] thawed"; see *also*, col. 6, lines 35-36, "serum which has been[...] thawed") (paraphrasing mine) to produce a melted solution of denatured lipoprotein (see e.g., col. 3, lines 57-58, "those lipoproteins which are associated with the turbidity");

3. mixing (see *e.g.*, col. 3, line 60, "reconstituted") a stabilizing agent (see *e.g.*, col. 3, line 66, "lipoprotein diluent"; see *also*, lines 67-68, "turbidity-potential lipoproteins"; see *also*, col. 4, line 48, "preservative"; see *also*, lines 50-52, "polyhydroxy cryoprotective agent, an antibiotic or antiseptic agent"; see *also*, lines 66-68, "ethylene glycol, diethylene glycol, propylene glycol and butylenes glycol, sorbitol, glucose, lactose and sucrose"; see *also*, col. 5, lines 5-6, "penicillin, gentimycin, tetracycline and bacitracin"; see *also*, line 17, "serum constituents"; see *also*, line 23, "carbonate compound"; see *also*, lines 30-31, "sodium bicarbonate, tris bicarbonate, and ammonium bicarbonate"; see *also*, lines 36-39, "sodium chloride, ammonium chloride, tris chloride, tris acetate, sodium acetate, and ammonium acetate, and tris-ethylenediamine tetraacetic acid") with the melted solution to produce a second solution; and

4. freeze-drying the second solution (see col. 6, lines 27-28, "the final serum standard to be lyophilized"; see *also*, col. 3, lines 49-50, "a serum standard which is conveniently stored prior to use"; see *also*, lines 31-32, "typical methods used for storage purposes include[...] lyophilization") (paraphrasing mine).

It would have been obvious for persons of ordinary skill to perform Proksch's & Bonderman's protocol on Kimura's denatured lipoprotein standard because Proksch & Bonderman say lipoproteins, in general, "cause significant turbidity upon lyophilization and reconstitution" (see col. 2, lines 34-37), which Proksch's & Bonderman's protocol apparently obviates by providing a lipoprotein standard that "does not result in a significant increase in the turbidity" (see col. 2, lines 46-50).

With respect to claim 67, Kimura *et al*. describe the claimed "FOH1a/DLH3" cell line (see Translation, paragraph [0006]).

Response to Arguments

In prior Office Action, claims 27, 29, 59, 62-64, 66 and 67 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kimura *et al*. (PTO 07-6676, English translation of JP 09-2881064) in view of Proksch & Bonderman (US 4,216,117).

In response, Applicants appear to argue that, although Proksch & Bonderman describe lipoprotein standards subjected to freeze-drying steps (see Applicants' reply, sentence bridging pp. 18-19), Proksch & Bonderman do not suggest steps of freezing and melting (see Applicants' reply, p. 19, last sentence).

Applicants' argument has been carefully considered but is not persuasive.

Proksch & Bonderman teach lost lipoproteins resulting from freeze-thawed sera (see *e.g.*, col. 3, line 59, "serum which is frozen and thawed"; see *also*, col. 6, lines 35-36, "serum which has been frozen and thawed"). Thus, since freeze-thawing sera was/is common practice (see col. 3, lines 31-32, "typical methods used for storage purposes include freezing"), a primary accomplishment of Proksch's & Bonderman's invention appears to have been its ability to reconstitute such lost lipoproteins in sera samples subjected to freezing and thawing (see *e.g.*, col. 3, line 59, "serum which is frozen and thawed"; see *also*, col. 6, lines 35-36, "serum which has been frozen and thawed").

Conclusion

No claims are allowable at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is (571)272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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